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(54) Title: ISOFLAVONOIDS FOR TREATMENT AND PREVENTION OF ALZHEIMER DEMENTIA AND REDUCED COGNITIVE FUNCTIONS

(57) Abstract

A method of treating or preventing, in a human patient, dementia of Alzheimer type, or age–related loss of cognitive function, said method comprising administering to said patient an isolated isoflavonoid selected from the group consisting of genistein, daidzein, biochanin A, formononetin, O–desmethylangolensin, glycitin, and equol, in an amount sufficient to produce a transient isoflavonoid concentration in the bloodstream of said patient of at least 100 nanomoles/L.

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ISOFLAVONOIDS FOR TREATMENT AND PREVENTION OF ALZHEIMER DEMENTIA AND REDUCED COGNITIVE FUNCTIONS

BACKGROUND OF THE INVENTION

The present invention relates to therapies for the prevention and treatment of dementia and reduced cognitive functions associated with advancing age.

It has long been recognized that dementia and diminished cognitive performance develop in persons over 65 years of age and these problems increase in frequency as the aging process advances. While these changes in cognitive behaviors are seen with the same frequency everywhere in the world, the types of dementing conditions differ in geographical areas. Thus, dementia of Alzheimer disease is more common than dementia of vascular disease in North America and Europe, while the dominant pattern in Japan is vascular dementia which is nearly twice as common as Alzheimer dementia. Another factor that influences cognitive functions in older women is the use of estrogen replacement therapy (ERT). The risk of developing Alzheimer disease and related dementia is less in women who use ERT after the production of their own estrogen hormones declines at the time of menopause. Cognitive function is improved in women who are given ERT for treatment of their dementia. Other drug treatments have been developed for Alzheimer dementia, but they are not fully effective and are associated with side effects. Safer and effective therapies for treating and preventing dementia and reduced cognitive function continue to be sought.

SUMMARY OF THE INVENTION

The invention features the use of isolated isoflavonoids, which are constituents of soy beans and other plants such as clover, to treat and prevent dementia of the Alzheimer type, as

well as other reduced cognitive functions associated with advancing age. Without being bound by any theory, it is believed that isoflavonoids have significant estrogenic activity, acting in the brain by enhancing neurotransmission and restoring synaptic density. It is believed that isoflavonoids are active in the brain at the same site as estrogen, exerting an estrogenic response. These compounds are safe and cause no significant side-effects. Isoflavonoids which may be administered according to the invention include genistein, daidzein, biochanin A, formononetin, O-desmethylangolensin, glycitin, and equol; these may be administered alone or in combination. The isolated isoflavonoid may be administered in any suitable form, e.g., in the form a plant extract rich in isoflavonoids or in the form of a purified or synthesized isoflavonoid. By "isolated" is meant the isoflavonoid is in a form which is more concentrated than the form in which it occurs naturally in plants. Treatment according to the invention is carried out using a therapeutic dietary product or a medicament form of one or more isolated isoflavonoid. The dietary product preferably includes a soy or plant extract enriched in isoflavonoids, provided in a palatable food carrier, e.g., a confectionary bar, biscuit, cereal or beverage. The medicament form preferably takes the form of a pill, tablet, capsule or powder, or a liquid or syrup formulation.

Other features and advantages of the invention will be apparent from the Detailed Description thereof, and from the claims.

DETAILED DESCRIPTION

Isoflavonoids are naturally occurring substances, found primarily in soy beans. These compounds can also be found in high concentrations in red clover and in lower amounts in many other types of plants. An isoflavonoid-containing fraction useful in the invention can be extracted from a soy or plant product. It is preferred that the isoflavonoids be extracted

and concentrated from soy bean or soy powder, but other plants such as clover can be used. Isoflavonoids are also available commercially in substantially pure form. The concentrated isoflavonoid is preferably included in a food carrier to form a dietary product. Any type of palatable carrier may be used, but as the isoflavonoid concentrate has a strong flavor, it is preferred that the carrier include suitable flavorings to impart a different, more palatable flavor. The dietary product may be any type of food product, e.g., a confectionary bar, biscuit, cereal or beverage.

It is preferred that the dietary product contain at least 20 mg/serving total isoflavonoids. The isoflavonoid concentrate included in the dietary product preferably includes a blend of isoflavonoids with genistein, daidzein, biochanin A, formononetin, O-desmethylangolensin, glycitin, and equol; these may be administered alone or in combination. Preferably, a dietary product containing the preferred dosage of isoflavonoids is consumed at least once per day, more preferably 2 times per day for more severe symptoms.

The isoflavonoid also can be administered, preferably in similar dosages, in medicament form, e.g., mixed with a pharmaceutically acceptable carrier to form a pill, tablet, capsule or powder, or a liquid or syrup formulation.

When isoflavonoids are fed to healthy American adults, the absorption into the bloodstream is 10 to 20% of the amount consumed. This produces blood levels of isoflavonoids 200 to 2000 times higher than the levels of the most active natural estrogen in women, estradiol. It is known that the estrogenic activity of isoflavonoids is about 1000 to 10,000 lower than that of estrogen contained in estrogen replacement therapy. These determinations indicate that consumption of isoflavonoids in dosages of 20 to 50 mg per day

provides blood levels with estrogenic activity in the range of that found with estrogen replacement therapy.

Other embodiments are within the claims.

We claim:

1. Use of an isolated isoflavonoid selected from the group consisting of genistein, daidzein, biochanin A, formononetin, O-desmethylangolensin, glycitin, and equol, in an amount sufficient to produce a transient isoflavonoid concentration in the bloodstream of a human patient of at least 100 nanomoles/L, in the preparation of a medicament for treating or preventing dementia of Alzheimer type, or age-related loss of cognitive function.

2. The use of claim **1** wherein medicament contains said isoflavonoid in an amount of at least 20 mg.

3. The use of claim **1** wherein there is administered to said patient at least one of genistein, daidzein, biochanin A, formononetin, O-desmethylangolensin, glycitin, or equol.

4. The use of claim **1** wherein said medicament is in the form of a non-naturally occurring dietary product.

5. The use of claim **4** wherein said medicament contains at least 20 mg/serving of said isoflavonoid.

6. The use of claim **4** wherein said dietary product is a confectionary bar.

7. The use of claim **4** wherein said dietary product is a cereal.

8. The use of claim **4** wherein said dietary product is a biscuit.

9. The use of claim **4** wherein said dietary product is a beverage.

10. The use of claim **4** wherein said medicament is in the form of a pill.

11. The use of claim **4** wherein said medicament is in the form of a tablet.

12. The use of claim **4** wherein said medicament is in the form of a capsule.

13. The use of claim **4** wherein said medicament is in the form of a powder.

14. The use of claim **4** wherein said medicament is in the form of a liquid or syrup.

INTERNATIONAL SEARCH REPORT

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PCT/US97/21863

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 9/08, 9/14, 9/20, 9/48, 35/78.
US CL :424/423, 195.1, 451, 464, 489, 422; 514/824, 879.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/423, 195.1, 451, 464, 489, 422; 514/824, 879.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,276,054 A (DIEZ et al.) 04 January 1994, entire document.	1-14
A, P	US 5,589,182 A (TASHIRO et al.) 31 December 1996, entire document.	1-14

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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